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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/917,710	08/26/1997	DANIEL P. BEDNARIK	1488.0450001	5107

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STERNE KESSLER GOLDSTEIN & FOX
1100 NEW YORK AVENUE NW
SUITE 600
WASHINGTON, DC 200053934

EXAMINER	
WEGERT, SANDRA L	
ART UNIT	PAPER NUMBER
1647	26

DATE MAILED: 10/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/917,710	BEDNARIK ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-29,38,39,49-58 and 60-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-29,38,39,49-58 and 60-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments, and/or Claims

The Information Disclosure Statement, received 26 November 1997 (Paper 4) and the Information Disclosure Statement, received 6 August 1998 (Paper 8), have been entered into the record. Claims 1-19, 30-37, 40-48 and 59 have been cancelled. Claims 20-29, 38, 39, 49-58 and 60-73 are being examined in the instant Application.

Due to the necessity of addressing new grounds of rejection, the finality of the previous Office action is hereby withdrawn. Applicant's Amendment after Final Rejection has been entered (Paper 19, 8/7/02).

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

35 U.S.C. § 112, second paragraph

The rejection of Claims 1, 6-10, 16f, 20(f)-20(l), 20(n), 29-34, 37-39, 48, 49(f)-49(g) and 59-63 under 35 U.S.C 112, second paragraph, as set forth on p. 3-4 of the previous Office Action (Paper No. 9, 3 December 1998), is *withdrawn* in view of the explanation by the Applicant and

in view of cancellation of claims that recited indefinite language related to "percent identity" and "subfragments" (Paper No. 11, 3 March 1999), and for cancellation of claims that recited indefinite language such as "substantially" and "subfragment" (Paper No. 11, 3 March 1999).

35 U.S.C. § 112, first paragraph

The rejection under 35 U.S.C. 112, first paragraph (scope), as set forth at p 4-6 of the previous Office Action (Paper No. 9, 3 December 1998) is *withdrawn* in view of the amendment which added SEQ ID NO's to independent Claims (Paper No. 11, 3 March 1999).

The rejection under 35 U.S.C. 112, first paragraph (written-description), as set forth at p 5-6 of the previous Office Action (Paper No. 9, 3 December 1998) is *withdrawn* in view of the amendment which added SEQ ID NO's to independent Claims (Paper No. 11, 3 March 1999) and which deleted recitations of "percent identity".

35 U.S.C. § 102 and 103.

The rejection of Claims 1, 6-10, 16 and 20-65 under 35 U.S.C. 102, or alternatively under 35 U.S.C 103, as set forth at p 6-7 of the previous Office Action (Paper No. 9, 3 December 1998), is *withdrawn* in view of the Amendment which introduced SEQ ID NO's into independent claims, cancelled claims directed to nucleotides encoding fragments of *IL1R AcM* and introduced precise hybridization language, so that remaining claims do not read upon all possible interleukin receptor accessory proteins (Paper No. 11, 3 March 1999).

Claim Rejections/Objections

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph-utility.

The following is a quotation of 35 U.S.C. 101:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-29, 38, 39, 49-58, 60-73 are rejected under 35 U.S.C. 101 because the claimed invention lacks a credible, specific and substantial asserted utility or a well-established utility.

The claims are directed to the polynucleotides encoding *IL-1R AcM* polypeptide, complementary nucleic acids, vectors comprising the polynucleotides, deposited host cells, and methods of recombinant expression of the peptide of SEQ ID NO: 2. The specification teaches recombinant expression of *IL-1R AcM* polypeptide and the results of an "Antigenic Index" algorithm (Jameson, et al, 1988, C.A.B.I.O.S, 4: 181-186) applied to the polypeptide sequence of SEQ ID NO: 2.

No well-established utility exists for newly isolated complex biological molecules. However, the specification asserts the following as credible, specific and substantial patentable utilities for the claimed polypeptide and the polynucleotides and recombinant methods used to express it:

1) To search for drugs as ligands or antagonists of the polypeptide encoded by the claimed polynucleotide,

2) For the production of antibodies,

3) To produce a variant or chimeric nucleotide or polypeptide,

4) To search for physiological activity of the claimed polynucleotide encoding the polypeptide, or its binding partners.

Each of these shall be addressed in turn:

1) To search for drugs as ligands or antagonists of the polypeptide encoded by the claimed polynucleotide. This asserted utility is credible and specific. However, it is not substantial. The specification does not characterize the polypeptide encoded by the polynucleotide of the claimed invention. Therefore binding sites, etc. are not identified. Significant further experimentation would be required of the skilled artisan to characterize the protein and search for ligands. There is no disclosure for example, of how to assay for ligand binding and possible transduction mechanisms. It is not known all classes of agonists to use or what measurements to perform. Since this asserted utility is not presented in mature form so it could be readily used in a real world sense, the asserted utility is not substantial.

2) For the production of antibodies. This asserted utility is credible and substantial, but not specific. Antibodies can be made to any polypeptide. However, if the specification discloses nothing specific and substantial about the polypeptide, both the nucleotide encoding the polypeptide and antibodies against the polypeptide have no patentable utility.

3) To produce a variant or chimeric nucleotide or polypeptide. This asserted utility is credible but not substantial or specific. Such assays can be performed with any polynucleotide. Further, the specification discloses nothing specific or substantial for the variant nucleotide and polypeptide that is produced by this method. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

4) *To search for physiological activity of the claimed polynucleotide encoding the polypeptide, or its binding partners*. Similarly, this asserted utility is credible and substantial. However, it is not specific. Such is performed for any peptide-ligand pair when the physiological role of each is not known. It is the definition of the type of further research that is required for either the claimed polynucleotide encoding the *IL-1R AcM* polypeptide to have patentable utility.

Claims 20-29, 38, 39, 49-58, 60-73 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 20-29, 38, 39, 49-58, 60-73 are directed to polynucleotide(s) encoding the *IL-1R AcM* polypeptide, complementary nucleic acids, vectors comprising the polynucleotides, deposited host cells, and methods of recombinant expression of the peptide of SEQ ID NO: 2.

The specification teaches the polypeptide of SEQ ID NO: 2 and the polynucleotides encoding it. The disclosure also presents the results of an algorithm called the *antigenic index*

that purportedly identifies antigenic determinants on a given polypeptide for which only the sequence is known (Figure 3 of Specification, for example). However, identifying possible epitopes on a polypeptide by use of a computerized algorithm is unreliable as far as correct identification of the epitopes, and does little to describe an enabled utility or function for the polypeptide. This was illustrated in a paper by Daniel, et al (1994, Virology, 202:540-549) in which nine antigenicity algorithms were applied to known polypeptides and compared with the resultant experimentally-derived epitopes. Features of the polypeptides such as hydrophobicity, contact with the protein surface and chain flexibility were poorly predictive of antigenicity or antibody binding sites (p. 541).

Furthermore, homology to known interleukin accessory proteins is not enabling for the polypeptide of the instant Specification. Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily

coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologues must have different molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan how to use the claimed polypeptides to make a biologically active transmembrane protein without resorting to undue experimentation to determine what the specific biological activities of the polypeptide are.

The specification does not teach the skilled artisan how to use the claimed polypeptide for any purpose. For example, there is no disclosure of particular disease states correlating to an alteration in levels or forms of the polypeptide such that the claimed polypeptides could be used as a diagnostic tool, or of the physiology of "knock-in" or "knock-out" animals, or of treatment protocols using the disclosed polypeptide, or of similar specifically-enabling experiments.

Therefore, the skilled artisan is not provided with sufficient guidance to use the claimed polypeptides for any purpose.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Due to the large quantity of experimentation necessary to determine an activity or property of the disclosed polypeptide such that it can be determined how to use the claimed polynucleotides and to screen for activity, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing that biological activity cannot be predicted based on structure, the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite particular biological activities, - undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion: Claims 20-29, 38, 39, 49-58 and 60-73 are rejected for the reasons listed above.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (703) 308-9346. The examiner can normally be reached Monday - Friday from 9:30 AM to 6:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Sandra Wegert
10/15/02

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER